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Original Communication

Correlations Between Macular Pigment Levels and Cognitive Performance Metrics in Children

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Abstract

Purpose: Macular pigment optical volume (MPOV) and cognitive function were characterized in children to explore the distributions of these parameters, as well as their consistency and potential associations. **Methods:** Baseline data from 65 healthy children aged 7–10 years (53.8% male, 78.5% white) enrolled in the Investigating Cognition and Ocular Nutrition in Children intervention study were analyzed. Demographic profiles were recorded, and participants underwent ophthalmic examination. Macular pigment (MP) was quantified using fundus autofluorescence imaging (Heidelberg Spectralis) at radii of 1° and 9°, expressed as central and total MPOVs, respectively. These parameters refer to the region where MP is largely concentrated and to the total of MP across the macula, respectively. Neurocognitive function was evaluated using the Cambridge Neuropsychological Test Automated Battery, which assesses attention, psychomotor speed, visual memory, and executive functions. Dietary intake was assessed using the Lutein and Zeaxanthin Food Frequency Questionnaire (LZQ) screening tool. Statistical correlation and regression analyses were conducted. **Results:** Mean central and total MPOVs were 333.05 ± 117.69 and 6903.54 ± 2925.81, respectively. Wide variation in MP distribution and concentration was observed across ethnicity, dietary carotenoid intake, and weight-specific differences, consistent with previously reported variability. As with MP, most variation in neurophysiological test performance was also consistent across demographic and ophthalmic characteristics. Across tasks, performance was correlated within the respective domains assessed. Domain-, sex-, and age-specific patterns showed no floor or ceiling effects, supporting the suitability of these measures in this cohort. Central MPOV was negatively associated with total errors in multitasking ($r = -0.24$, $p = 0.04$) and positively associated with memory task performance ($r = 0.26$, $p = 0.03$). After adjustment for demographic factors and dietary intake, children with higher MPOVs showed better attention ($\beta = -0.026$, $p = 0.03$) and cognitive flexibility ($\beta = 0.007$, $p = 0.02$) during multitasking. **Conclusion:** Despite the greater variability, our findings are broadly consistent with adult data and suggest that macular carotenoids (i) are likely involved in foundational cognitive processes, attention and cognitive flexibility, in children and (ii) likely support critical learning skills and knowledge acquisition. These insights are expected to guide future analyses and interventional research in children, a group that remains markedly less studied than adults.

Keywords: lutein; cognition; children; macular pigment (MP); macular pigment optical density (MPOD); macular pigment optical volume (MPOV); zeaxanthin

1. Introduction

The diet-derived carotenoids lutein, zeaxanthin, and *meso*-zeaxanthin selectively accumulate in the central retina, where they form macular pigment (MP) [1]. The density of MP in the macular area can be quantified *in vivo* in terms of macular pigment optical density (MPOD), which reflects long-term carotenoid intake and status. Higher MP levels have been linked to faster reaction times (RTIs), higher temporal vision, better visual performance, improved cognitive outcomes in adults, and better ocular health status [2,3,4]. Carotenoids also concentrate in brain regions involved in vision and cognition, such as the occipital and frontal cortex [5,6], and are thought to support the neural function through antioxidant and neuroprotective effects [7]. Despite being less abundant in the diet, lutein is present in the brain and retina at relatively high levels, thus possibly playing an important role in the neurocognitive function across the whole lifespan of an individual [8,9]. Associations between MP levels and visual/cognitive outcomes have been reliably established for adults but not children.

The accumulation of lutein and zeaxanthin in the retina and brain begins during perinatal development, gradually intensifying during early childhood and continuing during further life stages [10,11]. Thus, childhood is a critical period when these nutrients can influence cognitive and visual development [8,9,12]. However, very few studies have examined the corresponding associations in school-aged children [4,13]. The limited body of existing work

suggests that low MP levels are linked to brain activity patterns consistent with higher cognitive demand [14] and weaker cognitive performance, particularly in specific neuropsychological domains such as memory [15] and the executive function [16,17]. In infants, carotenoid status has been linked to neural activity patterns, selective transport mechanisms, and neurotransmitter pathways important for cognition, thus potentially playing an important functional role in the developing central nervous system [6,11]. Although past studies in this field differ in terms of the examined cognitive and visual functions and the magnitude of the established relationships, they consistently focus on adults and not children.

A further challenge to defining the relationship arises from the potential disparity among the many tasks designed to assess these functions and parameters, particularly macular carotenoid status. Mulder et al. [18] reported no significant association between lutein/zeaxanthin status (diet and serum) and cognitive performance in children aged 5–6 years. Rosok et al. [19] observed associations between carotenoid status and cognitive outcome for skin carotenoid levels but not for MP levels. This finding is controversial, since MP is a stronger neural biomarker [20,21]: MPOD is directly correlated with lutein and zeaxanthin concentrations in retinal and brain tissues [20], whereas skin carotenoid levels largely reflect short-term intake [2,22].

Moreover, evidence regarding MP measures in children has been conducted predominantly from studies conducted in the United States [13]. Given that diet is the main determinant of carotenoid status and that dietary patterns vary widely across regions because of ecological and cultural differences [23,24], such results may not be generalisable. Given that school age is a key stage for cognitive development, as supported by literature on learning, brain plasticity, and neurodevelopment [25,26], the above gaps require urgent attention. The above-mentioned inconsistencies and concerns highlight the need for a more precise characterisation of MP status in children and the exploration of its relationship with specific cognitive domains during childhood development.

This work investigates the relationship between MP levels and cognitive functions in children, using macular pigment optical volume (MPOV) as a more comprehensive and spatially broader representation of carotenoid status than MPOD. Given that MP is largely concentrated within the central 1° retinal eccentricity of the macula and the demonstrated importance of quantifying MP totality across the macula, we determine central and total MPOV as the sum of MP volume within radii of 1° and 9°, respectively [27,28]. We also examine multiple cognitive domains for demographic- and sex-specific differences and evaluate the distribution of cognitive functions across participants and their uniformity. These analyses form part of the Investigating Cognition and Ocular Nutrition in Children (ICONIC) trial, a pilot intervention study that seeks to advance the possible developmental benefit of a diet rich in macular carotenoids in supporting cognitive development during childhood and the design of a definitive trial.

2. Materials and Methods

2.1 Participants

Typically developing children aged 7–10 years (2nd–4th classes of primary school; n = 65, 53.8% males, 9.4 ± 0.9 years on average) were recruited from October 2023 to September 2024 from the Dublin area in Ireland. The participants were screened and excluded if diagnosed with any cognitive impairment or learning disability, conditions known to be associated with anomalous MP levels, underlying pathological or metabolic conditions, or other notable health problems. All participants and their legal guardians provided written assent and informed consent, respectively, at the beginning of the study visit. All procedures were approved by the Research Ethics Committee of Technological University Dublin (TU Dublin), reference number REIC-22-33, and adhered to the tenets of the Declaration of Helsinki. Information on the (1) specific sociodemographic factors of interest (age, sex, ethnicity, socioeconomic status (SES), parental education), (2) lifestyle factors (dietary intake), and (3) relevant health history (gestation, birth, medical, ocular) was collected using participant questionnaires. All data used herein were acquired during the first (baseline) visit before any intervention, and all procedures were performed during a single visit. Sampling, recruitment protocols, experimental techniques, and methods are detailed in **Supplementary Materials**. The subsection below briefly describes these procedures, focusing on cognitive, ocular, dietary, and anthropometric metrics.

2.2 Cognitive Function Assessment

A detailed description of the cognitive tests used to assess cognitive function is provided in the **Supplementary Materials**. The results of all measurements were expressed as raw scores. The following tests were administered.

The Cambridge Neuropsychological Test Automated Battery (CANTAB^{TM} software, Cambridge Cognition, Cambridge, UK; https://cambridgecognition.com/)—a computerised battery of cognitive tests—was administered to assess cognition aspects, with tests including the motor screening task (MOT), multitasking test (MTT), paired associates learning (PAL), spatial span (SSP), stop signal task (SST), and RTI (Fig. 1). The official CANTAB protocol was followed in all cases. The participants were tested in a room with ambient lighting and a quiet environment. For all the domain-specific cognitive tasks, fewer errors signified better cognitive performance. All tests were administered individually by the same trained investigator in one session.

The verbal fluency test was used to evaluate semantic and phonemic fluency [29]. In this test, the participants were asked to generate words in both phonemic (letter nam-

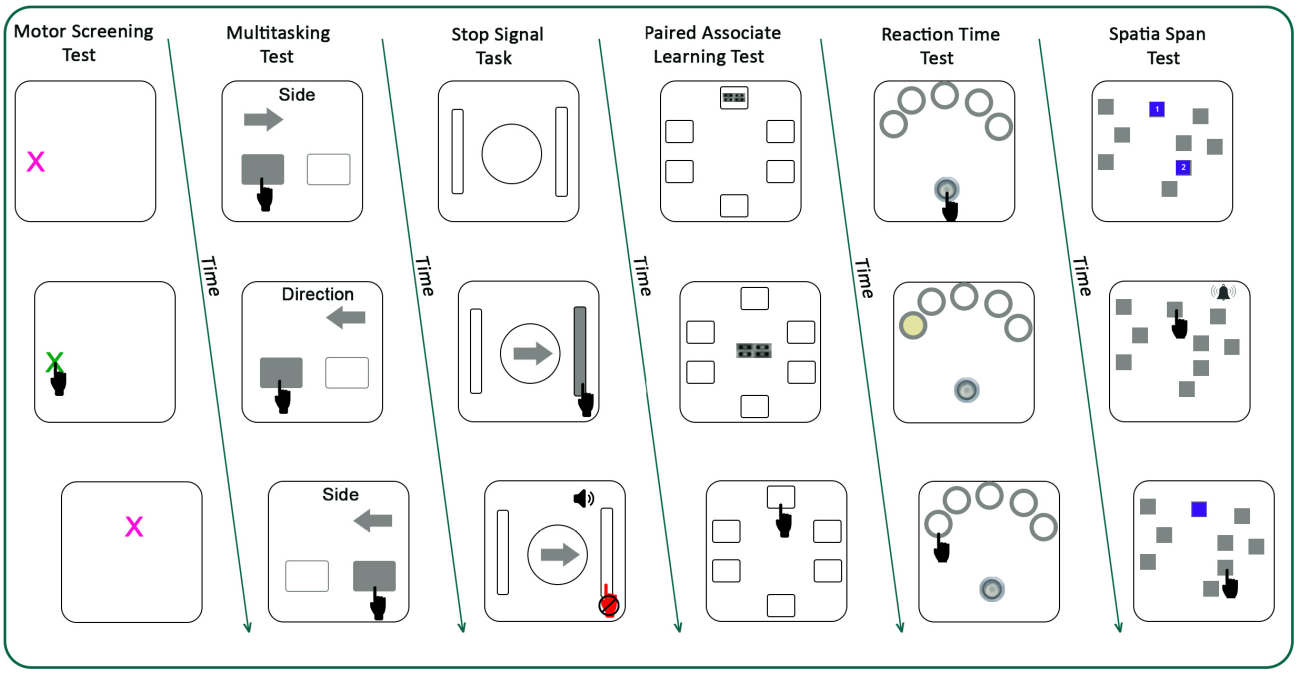

Fig. 1. Schematic of the six CANTAB subtests. Motor Screening Task: the first column illustrates colored crosses appearing sequentially at different screen locations. Participants touch each cross as it appears. Multitasking Test: the top and middle panels show congruent trials, whereas the bottom panel illustrates an incongruent trial. The cue displayed at the top of the screen ("Side" or "Direction") indicates the response rule, and participants select the corresponding virtual button. Stop Signal Task: the three panels illustrate the sequence of events during the task. Participants respond according to the direction of the arrow. The auditory beep in the bottom panel indicates presentation of the stop signal, and this requires a response inhibition. Paired Associates Learning: the top panel illustrates the learning phase, during which patterns are presented in different box locations. The middle panel shows a pattern displayed in the center of the screen for recall, and the bottom panel shows selection of the box corresponding to its original location. Reaction Time: participants initiate each trial by pressing and holding the response pad at the bottom of the screen. The middle panel shows presentation of the target stimulus (change in color of one of the circles to a yellow dot), and the bottom panel illustrates movement from the response pad to the target location. Spatial Span: the three panels illustrate a two-box level of the visuospatial memory task. Blue boxes indicate the sequence presented to the participant, with the end of the sequence signaled by an auditory tone (middle panel). Participants then reproduce the sequence in the same forward order.

ing) and semantic (animal naming) categories, which provided insights into cognitive flexibility skills. The total number of words named within 60 s was used to analyse test results.

These tests use stimuli randomisation and parallel modes to ensure performance stability and reliability. The built-in catch trials and exclusion of initial trials during scoring helped control practice and warming effects (transient poor performance at the start of the test) associated with repeated measurements in multiple test sessions. This intrasession control eliminated the need for additional sessions or test–retest assessments to quantify short-term variability within the chosen study protocol.

2.3 Visual Acuity and Reading Speed Assessment

Distance and near corrected visual acuity (VA) were measured under photopic illumination using a randomised letterset of the MultiQuity (MiQ 720; Sightrisk Limited, Waterford, Ireland) computerised logMAR (MAR = minimum angle of resolution) chart at 4 m and reduced logMAR chart (Precision Vision, Woodstock, IL, USA) at 40 cm, respectively.

The standardised Wilkins Rate of Reading Test at 40 cm without any overlay was used to assess reading speed (i.e., the time taken to correctly read a 150-word paragraph) and accuracy (i.e., the number of errors made while reading the paragraph) [30,31]. This test has good validity and reliability scores and is widely used. The outcomes were the total number of words read (reading speed) within or under 1 min. The test was performed twice using different paragraph versions, and the average and maximum values were recorded.

2.4 Macular Carotenoid Assessment

MP levels were assessed using fundus autofluorescence imaging performed using a dual-wavelength autofluorescence system (Heidelberg Engineering GmbH, Germany; Fig. 2). The principles of this technique are de-

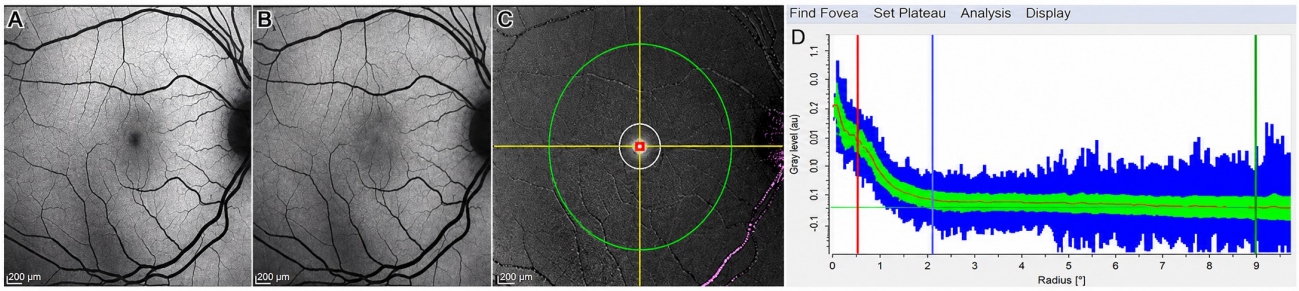

Fig. 2. Setup used for MP measurement using the Spectralis module (Heidelberg Engineering). Blue (486 nm) and green (518 nm) autofluorescence images were acquired simultaneously by the dual-wavelength SLO system of the device (A,B). Scale bar (bottom right overlay) = 200 µm (A,B). A differential topographic map of autofluorescence (C) was established using the in-built HEYEX software (Heidelberg Eye Explorer), and a radial density map of the MP distribution was created (C,D). Red, purple, and green concentric circles correspond to 0.5°, 2°, and 9° eccentricities, respectively. Red and green markers (D) can be moved to provide the relevant averaged optical density (MPOD) of the radius and sum of volume (MPOV) reading for the area of interest. MP, macular pigment; SLO, scanning laser ophthalmoscope.

scribed elsewhere [32,33]. Briefly, confocal scanning laser ophthalmoscope (SLO) with blue (486 nm) and green (518 nm) laser diodes is used [34]. The yellow MP absorbs blue light more than it does green light, which enables precise quantification by comparing autofluorescence emissions from the retinal pigment epithelium at these wavelengths. For familiarisation purposes, the participants were introduced to the MP measurement procedure, which was carefully explained to ensure comprehension before scanning and video recording. Following pupillary dilation, the participants were instructed to maintain their gaze on fixation stimuli in near-infrared reflectance mode to minimise involuntary eye movements prior to proceeding to the blue and green autofluorescence laser mode. A 30 s video of the simultaneous blue (486 nm) and green (518 nm) autofluorescence of the central field was recorded to ensure proper alignment. The HEYEX software (Heidelberg Eye Explorer version 1.9.13.0, Heidelberg Spectralis HRA OCT MultiColor device) (0.5% tropicamide eye drops, Bausch + Lomb) automatically averaged the images to create an MP density map, combining the results obtained at the two wavelengths. Reference eccentricity was defined at nine retinal degrees from the fixation point (where the MPOD is defined as zero). This procedure was repeated for each eye. All measurements were conducted by the same investigator according to a fixed protocol for all participants. Spatial mapping provided detailed insights into the distribution of MP across the retina at a relatively high resolution. The images from the video were carefully assessed for blinks or fixation loss for each participant before being processed to generate MP maps. To maintain independence of observations, if eligible images were available from both eyes, the dominant eye was selected by default. However, if the nondominant eye provided superior image quality, the nondominant eye was selected instead for statistical analyses.

2.5 Ocular Parameter Measurement: Biometry, Refractive Error, and Retinal Thickness

All subjects underwent a comprehensive ophthalmologic examination, including that of the fundus, to screen for ocular diseases. Iris colour was graded as blue, green, or brown using a validated scale [35]. Axial length (AL) and other ocular biometric parameters, including anterior chamber depth (ACD), corneal curvature, corneal diameter, and central corneal thickness (CCT), were measured using a low-coherence interferometry biometer (Aladdin HW3.0, Visia Imaging S.r.l., San Giovanni, Valdarno, Italy). Five readings of axial length were obtained per measurement, and the mean was recorded. Retinal thickness and retinal volume were measured through dilated pupils (0.5% tropicamide eye drops) using Swept-source optical coherence tomography (OCT) (Topcon DRI-OCT Triton Plus, Topcon Corporation, Tokyo, Japan). Central retinal thickness was defined as the distance between the internal limiting membrane and the presumed retinal pigment epithelium at the fovea. Noncycloplegic and cycloplegic autorefractions were performed to obtain refractive status, then the spherical equivalent refraction (SER) was determined from sphere and one-half the cylinder powers.

2.6 Dietary Carotenoid Assessment

The dietary intake of lutein and zeaxanthin was estimated using a crude carotenoid screener (lutein/zeaxanthin (L/Z) screener) developed by Elizabeth Johnson (Tufts University, Boston, Massachusetts). The screener provided a dietary score of 0–75, with intake categorised as low (category 1, L/Z intake score 0–15, ≤2 mg/day), medium (category 2, L/Z intake score 16–30, 3–13 mg/day), or high (category 3, L/Z intake score 31–75, >13 mg/day). This tool is described in detail in previous studies [21,36].

2.7 Anthropometrics

Height and weight were recorded to calculate the body mass index (BMI). The BMI and BMI-for-age percentile (BMI%) were calculated according to the guidelines set by the Centers for Disease Control and Prevention [37]. Measurements were taken without shoes and while wearing lightweight clothing. A stadiometer (Seca 123, Hamburg, Germany) and calibrated scale (Tanita Corporation, Tokyo, Japan) were used to measure height and weight, respectively.

2.8 Statistical Analyses

Continuous variables were expressed as means (standard deviations (SDs)) or medians (interquartile ranges), with their distributions assessed by the one-sample Kolmogorov–Smirnov test and visual inspection (Q–Q plots, histograms). Categorical variables were reported as frequencies and percentages.

Given the biological, cognitive, and behavioural variations between males and females [38], sex differences were evaluated using *t*-tests or Mann–Whitney U tests for continuous variables and chi-square or Fisher's exact tests for categorical variables. Analysis of variance or Kruskal–Wallis tests were used for comparisons across multiple groups and repeated measures, as appropriate. Pearson's correlation was used for normally distributed variables, while Spearman's rank correlation was used for nonnormal data. Univariate and multiple linear regression models were used to examine relationships between MPOV and visual/cognitive measures. Covariates for multivariate analyses were selected based on statistically significant bivariate correlations or a priori in theoretical or clinical relevance. Variance inflation factor (VIF) analysis was used to test for the multicollinearity of variables in the regression (1/(1-model R^2; VIF >5)) [39]. Sensitivity analyses were performed by comparing estimated marginal means with raw measures. The estimated marginal means were consistent across MP measures and cognitive scores, with no significant interaction effects observed within measures and sex.

Outliers (>3 SDs from the mean) were removed from all variables in the dataset unless they were within allowable outcome limits for cognitive measures. For the ophthalmic assessments, complete data were available for 63 of 65 participants and outliers for one participant were removed from all continuous data under the ocular characteristics.

The open-source statistical package R (R Foundation for Statistical Computing, Vienna, Austria; https://www.r-project.org) was used, and an alpha threshold of 0.05 was employed in all statistical analyses. Owing to the largely a priori relationships and exploratory analyses, corrections for alpha-error were not applied.

3. Results

No significant differences in all ocular parameters were observed between the left and right eyes (all $p > 0.05$). The dominant eye was subsequently selected for analyses, unless the measurements in the nondominant eye provided a better signal strength index or higher-quality scan during the image acquisition for retinal measures.

3.1 Baseline Participant Characteristics

The characteristics of the 65 participants are summarised in Table 1. The mean age was 9.4 ± 0.9 years (range: 7.6–10.9 years). Student's *t*-test revealed no significant differences ($p > 0.05$) between males and females in terms of baseline demographic characteristics. The participants were categorised into racial groups, namely Caucasians (66%), African (6%), Asian (6%), Hispanic (12%), and mixed (9%). Owing to the limited representation of participants from other racial groups, ethnicity was dichotomised into "white" and "nonwhite" for follow-up analysis. Although the recruitment goal was to reach a wider demographic, only eight participants were from rural areas. Similarly, the number of SES-disadvantaged participants was limited, signifying a clear SES disparity bias. No significant differences between males and females were observed in terms of birth, breastfeeding, and lifestyle measures. The mean reading speed was 108.6 ± 22.6 words per minute (range: 48–158 words per minute), with boys at 103.2 (22.6) words per minute and girls at 112.7 (21.1) words per minute. However, this difference was not statistically significant ($p = 0.08$).

3.2 Distribution of MP Levels

Independent *t*-tests revealed no statistically significant differences between male and female participants ($p > 0.05$) in terms of central and total MPOVs, which averaged to 333.05 ± 117.69 (95% confidence interval (CI): 303.89–362.21) and 6903.54 ± 2925.81 (95% CI: 6163.51–7641.57), respectively. A histogram of the data is provided in Fig. 3. For central and total MPOVs, the coefficients of variation (COVs) were 0.35 and 0.43, respectively, and the intraclass correlation coefficients (ICCs) were 0.73 and 0.91, respectively. Both eccentricities were not significantly correlated ($r = 0.14$, $p = 0.24$). Approximately 45% and 55% of participants had below-mean central and total MPOVs, respectively.

3.3 Relationships Between MP Levels and Participants' Characteristics

The bivariate analysis of MP level by participant characteristics revealed that central MPOV differed significantly by ethnicity, with white participants exhibiting higher levels (t (21.17) = 3.52, $p = 0.002$, 95% CI: 46.73–180.90). Although no statistical difference existed between weight status (normal weight, overweight, obese) and MPOV (F (2, 62) = 3.05, $p = 0.05$), obese (≥95th percentile) participants exhibited lower MPOVs. A similar trend was observed for birth term status, with participants born preterm ($n = 9$) having lower MPOVs (t (11.15) =

Table 1. Characteristics of study participants according to sex.

Characteristics	All *n* = 65	Male *n* = 35	Female *n* = 30	*p*
Mean age in years (SD)	9.4 (0.9)	9.3 (1.0)	9.5 (0.8)	0.40[a]
Race *n* (%)				
Caucasian	43 (66.2)	22 (62.9)	21 (70.0)	0.42[b]
African	4 (6.2)	1 (2.9)	3 (10.0)	
Asian	4 (6.2)	3 (8.6)	1 (3.3)	
Hispanic	8 (12.3)	6 (17.1)	2 (6.7)	
Mixed	6 (9.2)	3 (8.6)	3 (10.0)	
Ethnicity *n* (%)				
White	51 (78.5)	28 (80.0)	23 (76.7)	0.74[c]
Nonwhite	14 (21.5)	7 (20.0)	7 (23.3)	
Living environment *n* (%)				
Urban	57 (87.7)	31 (88.6)	26 (86.7)	1.00[b]
Rural	8 (12.3)	4 (11.4)	4 (13.3)	
SES *n* (%)				
Advantaged	57 (87.7)	29 (82.9)	28 (93.3)	0.37[b]
Disadvantaged	8 (12.3)	6 (17.1)	2 (6.7)	
Parental education *n* (%)				
No tertiary education	11 (16.9)	6 (17.1)	5 (16.7)	1.00[c]
Tertiary education (diploma, first degree, or higher degree)	54 (83.1)	29 (82.9)	25 (83.3)	
Anthropometry and dietary measures				
BMI% (SD)	54.7 (29.1)	52.3 (26.7)	59.9 (29.9)	0.47[a]
BMI category *n* (%)				
Normal weight (≥5th and <85th)	49 (75.4)	25 (71.4)	24 (80.0)	0.28[b]
Overweight (≥85th and <95th)	9 (13.8)	7 (20.0)	2 (6.7)	
Obese (≥95th)	7 (10.8)	3 (8.6)	4 (13.3)	
[d]Estimated lutein, zeaxanthin and *meso*-zeaxanthin dietary intake score (SD)	17.5 (12.9)	17.3 (11.9)	20.3 (16.2)	0.46[a]
Reading speed in words per minute (SD)	108.6 (22.6)	103.2 (22.6)	112.7 (21.1)	0.08[a]
Mean MP level (SD)				
MPOV 1°, i.e., central MPOV	333.05 (117.69)	327.50 (121.93)	339.53 (114.26)	0.68[a]
MPOV 9°, i.e., total MPOV	6903.54 (2925.81)	6837.84 (3264.12)	6978.03 (2669.95)	0.84[a]

[a]Independent *t*-test. [b]Fisher's exact test. [c]Chi-square test. The significance threshold was set at $p < 0.05$ (two-tailed). [d]Lutein and Zeaxanthin dietary intake: ≤2 mg/day (0–15 score); medium intake, category 2: 3–13 mg/day (16–30 score); high intake, category 3: >13 mg/day (31–75 score). SES, socioeconomic status; BMI, body mass index; BMI%, BMI-for-age percentile.

2.05, $p = 0.06$, 95% CI: –143.82–4243.19 for total MPOV). Total MPOV significantly differed between breastfed (n = 57) and formula-fed (n = 8) children (t (11.55) = 2.42, p = 0.03, 95% CI: 174.53–3460.82) and was positively correlated with breastfeeding duration (r (57) = 0.35, p = 0.0002). It should be noted that there were relatively smaller numbers of obese and formula-fed children; comparisons should be interpreted cautiously. Most participants (51%) had a low carotenoid dietary intake score (0–15, ≤2 mg/day), and only 12% had a high score (31–75, >13 mg/day). The mean carotenoid intake score was 17.5 ± 12.9, ranged from 0 to 58, and was positively correlated with total MPOV (r = 0.39, p = 0.001).

Participants were predominantly emmetropic (68%) and had blue iris colouration (45%). MPOVs were consistent among iris colouration and refractive status ($p > 0.05$), possibly because of the considerable overlap observed. The ocular parameters were as follows: mean VA, −0.10 ± 0.10 (range: −0.21–0.14), mean AL, 23.2 ± 0.8 mm (range: 21.6–25.7 mm), mean SER, −0.10 ± 1.80 diopters (range: −5.00–5.75 diopters), mean ACD, 3.5 ± 0.3 (range: 2.6–4.2 mm), and mean CCT, 550 ± 35 (range: 443–605 µm). The mean foveal thickness was 243.1 ± 23.3 µm (range: 186.0–284.0 µm). Central MPOV was positively correlated with axial length (r(63) = 0.258, p = 0.03) and subfoveal thickness (r(63) = 0.340, p = 0.006).

3.4 Cognitive Measures

All participants completed all cognitive assessments. Females achieved significantly higher scores only on memory tasks (PAL memory score, t (62) = −1.72, p = 0.03), and no other significant differences in performance were

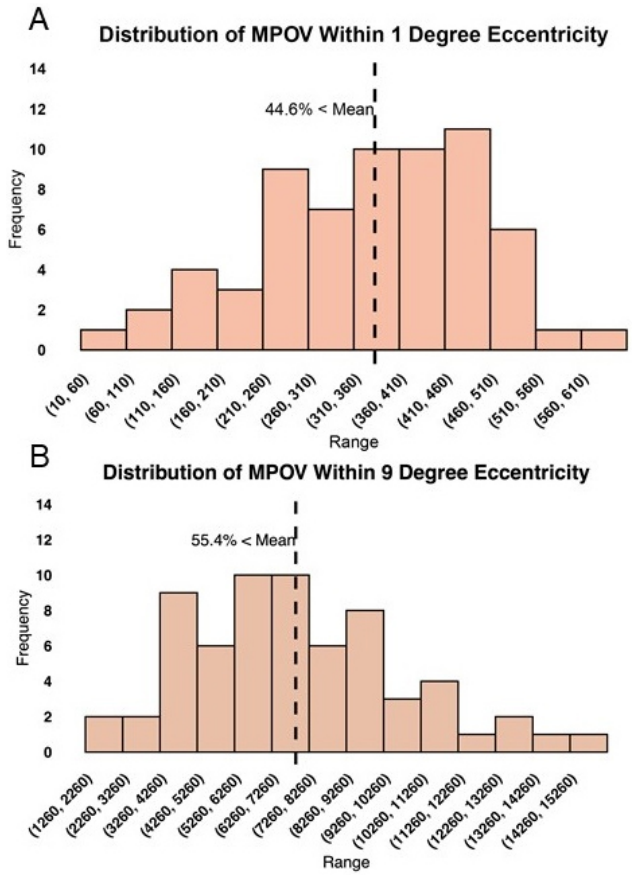

Fig. 3. Distribution of (A) central and (B) total MPOVs. The black dotted line indicates the mean MPOV for a given eccentricity, illustrating the difference in distribution modality.

observed between sexes. Age was significantly correlated with phonemic fluency (r = 0.32, p = 0.008), some RTI measures (r = −0.29, p = 0.01), attention (r = −0.41, p = 0.0007), working memory (r = 0.45, p = 0.0001), and inhibition measures (r = −0.26, p = 0.03) and was therefore included as a covariate in subsequent analyses. Phonemic fluency was lower among SES-disadvantaged participants. Finally, higher BMI% was associated with slower performance on tasks measuring processing speed (RTI simple mean: r = 0.25, p = 0.03) and attention (MTT total incorrect: r = 0.28, p = 0.02). This association was not evident in categorised BMI classifications. Additionally, the distribution of task scores showed no appreciable clustering at the minimum or maximum score limits. Within the sex-, age- and domain-specific performances, there was no evidence of floor or ceiling effects when the proportion of participants who achieved the highest and lowest possible scores were evaluated.

Across tasks, performance on short-term working memory (SSP: forward span) was significantly correlated with semantic fluency (r = 0.25, p = 0.03), phonemic fluency (r = 0.34, p = 0.005), and memory scores (PAL total errors, r = −0.32, p = 0.009; PAL first attempt, r = 0.27, p = 0.03). The same pattern was observed for statistically significant correlations within the processing speed domain (MOT latency and RTI simple mean). A similar pattern emerged for error scores in multitasking (MTT total incorrect) and PAL tasks (PAL first attempt: r = 0.38, p = 0.002). Regarding attention measures, the RTI five-choice was not associated with the MTT total incorrect score. The probability of slowing after an error or success in the inhibition task did not correlate with any accuracy or latency measure. Overall, these correlations indicated that different latencies within the processing speed domain were interrelated, as were accuracy measures and memory scores; however, comparisons between latency and accuracy did not demonstrate a meaningful relationship.

Bivariate correlation analysis revealed that central MPOV was significantly correlated with short-term working memory (SSP forward span: r = 0.26, p = 0.03) and total incorrect score on multitasking (MTT total incorrect: r = −0.24, p = 0.04), which indicated that higher MP levels were associated with better working memory and fewer inattention errors. Central MPOV also exhibited a trendwise correlation to post-error slowing in SST. A correlation with borderline significance was observed between a slower response after an error in the inhibition task and central MPOV (p = 0.05). Total MPOV was not significantly correlated with any of the tasks but showed a trendwise positive correlation with RTI five-choice movement and MTT incongruency cost. A detailed analysis for these measures is provided in **Supplementary Table 2**.

Regression analysis was conducted to examine the association with MPOV on significant and trendwise correlations (Table 2). Following adjustment for demographic factors and dietary intake, central MPOV approached borderline significance for working memory scores (β = 0.003, R^2 = 0.27, p = 0.05) and negatively predicted incorrect scores in multitasking (β = −0.026, R^2 = 0.27, p = 0.03) (Fig. 4A). During multitasking, the response delay time was longer for conflicting stimuli (incongruent trial) but shorter for matching stimuli (congruent trial) and was positively predicted by total MPOV (β = 0.007, R^2 = 0.08, p = 0.02) (Fig. 4B). Altogether, higher MPOVs were associated with fewer errors but slower response when processing conflicting stimuli, which suggests an association with executive functioning. No other instances of significance were found.

4. Discussion

The present study utilised robust protocols, in line with previous research, and achieved relatively high consistency, providing a comprehensive overview of MP and cognition measures, their distribution, and their variation across different sociodemographic, dietary, anthropometric, and ophthalmic factors in children.

Owing to the asymmetric spatial distribution of MP, MPOV was used as a quantitative metric. MPOV distributions were broadly dispersed, the histogram envelope

Table 2. Results of multivariate regression predicting the performance on cognitive tasks and MPOVs by retinal eccentricity.

Domain of cognitive function variables	Central MPOV			Total MPOV		
	Estimate β (95% CI)	p	R^2	Estimate β (95% CI)	p	R^2
Attention						
RTI median five-choice movement	0.015 (−0.076 to 0.107)	0.74	0.06	0.003 (−0.001 to 0.007)	0.11	0.10
MTT total incorrect	−0.026 (−0.050 to −0.002)	**0.03**	0.27*	0.000 (−0.001 to –0.001)	0.82	0.21*
Working memory						
SSP: Forward span length	0.003 (0.000 to 0.006)	0.05	0.27*	-7.18×10^{-6} (0.000 to 0.000)	0.90	0.23*
Inhibition						
SST posterror slowing	0.017 (−0.006 to 0.040)	0.13	0.15	0.000 (−0.001 to 0.001)	0.53	0.13
Cognitive flexibility						
‡MTT median incongruency cost (log-transformed variable)	−0.035 (−0.168 to 0.145)	0.65	0.09	0.007 (0.001 to 0.014)	**0.02**	0.08*

Association was estimated using multivariate regression. Analysis included age, sex, BMI%, and an estimate of macular carotenoid dietary intake. Estimates are presented as β (95% CI) and back-transformed β (95% CI) for log-transformed variables. β - nonstandardised beta; regression coefficient, *The significance threshold was set at $p < 0.05$ (two-tailed). RTI, reaction time; ‡MTT, median incongruency cost (log-transformed variable); SSP, forward span length; SST, post-error slowing. The significance threshold was set at $p < 0.05$ (two-tailed), bold values indicate statistically significant findings ($p < 0.05$). Asterisks (*) indicate statistically significant overall regression models.

approximated normal curves, with only a slight skew observed toward lower indices, which suggests the possibility of large differences in lutein and zeaxanthin status among participants. An important aspect of our findings is the substantial interindividual variation in MP distribution, a pattern consistently reported in normal adults. This indicates that variability is a stable characteristic across age groups. In addition, significant differences between the central and total MPOVs were evident. The finding that central MPOV does not always correlate with total MPOV is consistent with previously published distribution patterns [27,28,40]. The MPOV magnitudes and distributions strongly support measure completeness and data consistency.

However, most previous studies using autofluorescence imaging mainly targeted adults, not children. Herein, we found that the measure demonstrates adequate reliability in children despite the wide variation and distribution. Given that dual-wavelength fundus autofluorescence–based MPOD estimation depends on detectable lipofuscin fluorescence, low lipofuscin levels in children may affect the signal-to-noise ratio and thereby influence the precision of MPOD estimates. However, as MPOD is derived from the relative attenuation of two excitation wavelengths rather than absolute intensity [41], the method remains valid for quantifying MP distribution in children and eliminates this concern, provided that sufficient autofluorescence is detectable (as demonstrated in younger cohorts [42,43]). Moreover, the uniformly low lipofuscin level in children [43] may reduce the heterogeneity that confounds autofluorescence interpretation in older eye [44], providing stable excitation and attenuation for assessing MP distribution. Low autofluorescence signals may introduce additional variability, and MPOD values should be interpreted with caution. Nonetheless, autofluorescence-based MP assessment is feasible and reproducible across a broad age range [33,34,45], which supports its continued use as a practical noninvasive tool in paediatric research [46]. Although the present study cannot directly address the reliability of MP measurement via fundus autofluorescence in children, the detailed dual-wavelength autofluorescence images, ICCs, and COVs obtained herein, as well as the use of a single rater for acquisitions, corroborate the utility of this method within the examined age cohort, as noted earlier [46]. Additional work is needed, and future studies incorporating complementary measurement techniques may further strengthen validation in paediatric populations.

Differences across race, ethnicity, parent education, weight status, birth history, and ocular characteristics commonly noted in the literature were also identified in the ICONIC cohort. Whereas the MP measures displayed high spatial reproducibility patterns with no sex-dependent differences, cognitive parameters differed by sex, in agreement with previous findings [47,48]. Future ICONIC measurements should determine whether these differences relate to greater disparities within this sample. Additionally, we identified consistency across many cognitive domains, including processing speed, memory, and cognitive flexibility, which require further contextualised analyses. Fi-

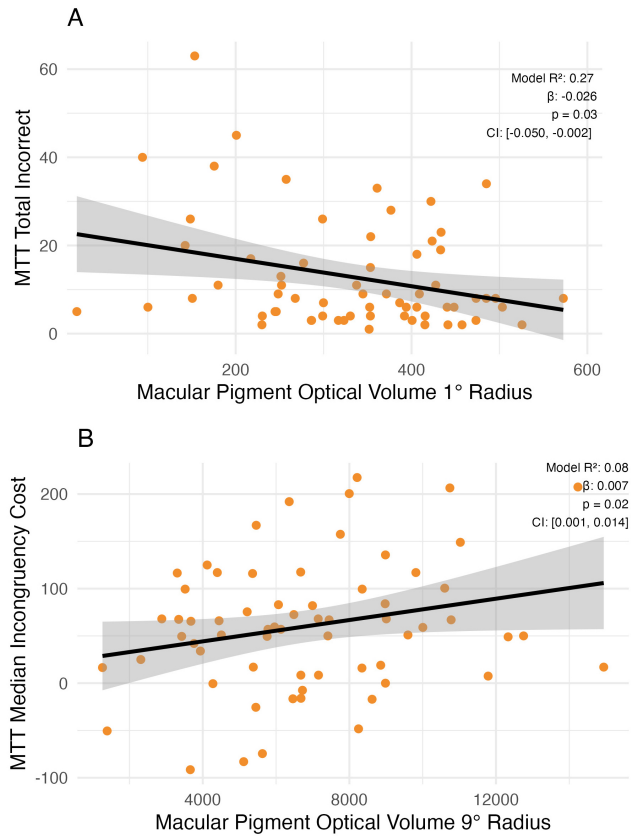

Fig. 4. Association between MP status and performance during MTT. (A) Total incorrect, errors calculated across all trials and representing the number of trials where outcome was an incorrect response; (B) median incongruency cost, defined as the median latency score for incongruent trials versus congruent trials. Each data point signifies a single participant. Solid black line denotes the regression line, and the shaded area surrounding it indicates the 95% confidence interval for the regression, as detailed in Table 2 above.

nally, we highlighted how participants' functional measures relate to MP status, thereby facilitating the further characterisation of this study sample.

The baseline analysis of the ICONIC cohort revealed that higher MPOVs were associated with fewer errors during multitasking and slower responses during the processing of conflicting information. A trend toward better short-term working memory was also observed. While modest and novel in this age group, the observed associations are consistent with a small body of paediatric research linking macular carotenoids to cognitive outcomes. For example, lower MP levels have been related to reduced efficiency in cognitive tasks and higher neural indices of cognitive load [14], with specific links reported for memory [15] and executive processes [16,17]. Such findings, together with evidence that retinal MP levels correlate with lutein and zeaxanthin concentrations in the brain [6,11], provide a plausible explanation for why children with higher MPOVs in the present study demonstrated advantages in tasks requiring attention and cognitive flexibility. These associations provide a hypothetical basis to further study the relationships between macular carotenoids and executive processes such as selective attention and cognitive flexibility in school-aged children.

The clearest association was observed for cognitive flexibility, a core component of the executive function that reflects the ability to shift attention and adapt response strategies in the face of conflict and requires substantial cognitive resources to inhibit irrelevant information. Cognitive flexibility is considered foundational for academic skills, closely correlating with prereading and premath development in children [49,50], and builds on the development of inhibition and working memory [51,52]. Although MPOV was probably associated with cognitive flexibility, no significant associations were found with other executive function measures after controlling for covariates. This pattern limits a broad interpretation of executive involvement but is consistent with previous findings that have linked MP status with specific aspects of memory [15] and inhibition [14,17]. Interestingly, the consistency of performance across the selected tests assessing the same underlying cognitive domain, along with the corresponding variances, supports the relative stability of the measures and their domains.

The divergence across different domains may relate to differences in task demands. Relational memory, for instance, is more closely aligned with the hippocampal function, whereas attentional inhibition depends on selective attention processes rather than inhibitory control *per se* [53]. In our cohort, correlations were modest, with cognitive flexibility accounting for ~8% of the variance. These weak associations may partly reflect the fact that the MPOVs observed herein were lower than those previously reported for children and adults [27,32]. Typically, studies in children have reported minimal effects, as follows from the usually modest regression and correlation coefficients (R^2 = 0.05–0.15; r = 0.09–0.28) [13,54], which contrasts with the consistently stronger effects reported for adults (r = 0.18–0.45) [54]. However, our findings in children in corroboration with previous studies are remarkable, as prior research in generally healthy children often reports null associations between nutritional biomarkers and behavioral outcomes when no underlying deficiencies are present [55,56]. Given the known roles of macular carotenoids in neural functioning [9,57,58], stronger associations are likely to emerge at higher carotenoid levels or in intervention studies. One should also consider developmental variability in our age group, which may dilute cross-sectional associations but offer greater scope for detecting change over time. Importantly, our data extend these observations by highlighting MPOV, a broader spatial measure of MP, as a potentially useful biomarker of cognition-relevant carotenoid status in children.

The physiological variation in lutein, zeaxanthin, and *meso*-zeaxanthin composition across the retina is well established [1,59,60]. MPOV 1° (central MPOV) represents the integrated pigment level within a circular area of 1° radius, which is enriched in zeaxanthin and may feature a lutein:zeaxanthin ratio of up to 1:2.4, whereas MPOV 9° (total MPOV) captures the pigment distributed across the broader parafoveal region, where the carotenoid profile shifts toward lutein dominance (lutein:zeaxanthin ratios above 2:1). In this context, MPOV is only used as a surrogate measure of brain lutein and zeaxanthin concentrations; however, the absence of consistent associations with cognitive tasks across central and total MPOVs is also worth noting. Central MPOV was linked more strongly with multitasking accuracy, whereas total MPOV showed associations with incongruency cost. This variability echoes the fact that different eccentricities may relate differently to cognitive measures [21,61], suggests that the spatial distribution of MP may be functionally relevant, and supports the use of broader measures such as MPOV in paediatric research.

Although exploratory, our findings justify the continued and more comprehensive examination of the potential role of macular carotenoids in supporting executive processes. Lutein and zeaxanthin are highly concentrated in the prefrontal cortex [11,62], a region critical for attention shifting and multitasking [63,64]. The antioxidant and anti-inflammatory properties of these species, together with imaging study–based evidence that higher carotenoid status improves neural efficiency [58,65], may provide a biologically plausible explanation for the observed associations. Supplementation trials in adults have demonstrated benefits for memory and cognitive control [54,66], although the possibility of achieving effects in children, a group with high neuroplasticity [25,26], remains to be established.

The key strengths of this study include the use of MPOV, which captures the spatial distribution of MP beyond single-point measures, and the application of a comprehensive, validated cognitive battery with strong internal validity. However, the cross-sectional study design limited causal inference, and the sample size provided only modest power. Multiple comparisons were not corrected for, and significant associations should therefore be viewed as exploratory. Although we ensured the use of measures with superior reproducibility and repeatability indices, we cannot speak on temporal stability or test–retest reliability in the cognitive and noncognitive or discount the possibility that unmeasured potential confounders (fatigue, motivation) contributed to within-person variations. Despite these challenges, the study maintained a high degree of objectivity in the examined measures, which have been reported to be clinically significant in paediatric research in numerous studies. The cohort was predominantly socioeconomically advantaged and from a single geographic region, which restricts generalisability because of the known regional variation in diet and carotenoid intake [24,67]. Dietary intake was assessed using a brief screener that does not reflect absorption or bioavailability.

Within the abovementioned constraints, our findings add to the limited evidence base linking MP levels with cognition in childhood and suggest that executive processes, particularly cognitive flexibility, may be sensitive to macular carotenoid status. Future work should prioritise longitudinal and interventional studies with larger and more diverse cohorts to clarify whether improving carotenoid status during childhood translates into measurable cognitive benefits. Importantly, our data extend these observations by highlighting MPOV—a broader spatial measure of MP—as a potentially useful biomarker of cognition-relevant carotenoid status in childhood.

5. Conclusions

MP levels, cognition, and clinical characteristics were measured in typically developing children aged 7–10 years. Higher MPOVs were associated with fewer errors in multitasking and altered response dynamics under conflicting conditions, which are measures of executive functioning. These findings highlight cognitive flexibility and attention as potential domains of interest for future research and underscore the importance of longitudinal and interventional studies for determining whether improving macular carotenoid status may enhance cognitive performance in children.

Abbreviations

AL, Axial length; ACD, Anterior Chamber Depth; BMI, body mass index; BMI%, BMI-for-age percentile; CANTAB, Cambridge Neuropsychological Test Automated Battery; CCT, Central Corneal Thickness; CI, confidence interval; COV, coefficient of variation; ICC, intraclass correlation coefficient; ICONIC, Investigating Cognition and Ocular Nutrition in Children; L/Z, lutein/zeaxanthin; MAR, minimum angle of resolution; MOT, motor screening task; MP, macular pigment; MPOD, macular pigment optical density; MPOV, macular pigment optical volume; MTT, multitasking task; PAL, paired associates learning; RTI, reaction time; SD, standard deviation; SER, Spherical Equivalent Refraction; SES, socioeconomic status; SLO, Scanning Laser Ophthalmoscopy; SSP, spatial span; SST, stop signal task; VA, Visual acuity; VIF, Variance Inflation Factor; OCT, optical coherence tomography.

Availability of Data and Materials

All data reported in this paper may be made available from the corresponding author upon reasonable request and with appropriate institutional request and ethical approvals.

Author Contributions

EED: conceptualisation, methodology, formal analysis, investigation, data curation, project administration, visualisation, writing—original draft preparation, writing—review and editing. JSB: methodology, data curation, writing—review and editing. AS: methodology, data curation, writing—review and editing. JL: supervision, conceptualisation, methodology, formal analysis, investigation, data curation, supporting original draft writing, reviewing and editing. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors participated sufficiently in the work and agreed to be accountable for all parts of it.

Ethics Approval and Consent to Participate

The study was conducted in accordance with the Declaration of Helsinki. The research protocol was approved by the This study was approved by the Research Ethics Committee of Technological University Dublin (TU Dublin) (Ref No. REIC-22-33), and all participants were provided written informed consent prior to data collection (informed consent was obtained from all participants' parents/legal guardians, and child assent was obtained on the day of testing).

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Conflicts of Interest

The authors declare no conflicts of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.31083/IJVNR50214.

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